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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,042	10/24/2003	Nurit Kalderon		1520

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,042	KALDERON, NURIT	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/03,1/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The Information Disclosure Statement, received 24 October 2003, and the Information Disclosure Statement, received 26 January 2004 have been entered into the record.

Applicant's election of Invention I (Claims 1-6, 8-13, 15-20 and 22-27), in the Paper of 8 January 2007, is acknowledged. The Applicant traversed the Restriction requirement, arguing that the methods of the two Inventions are not mutually-exclusive, as the examiner had argued. The examiner agrees that the claims that recite administration of interferon "at day 11 or later" do in fact overlap in scope with the claims that recite "at the 4th week or later." Thus, invention II will be re-joined with Invention I for the instant examination. It should be kept in mind that if the examiner finds one of the inventions unpatentable over the prior art, the argument by the Applicant that the methods are not patentably distinct may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Claims 1-28 are under examination in the Instant Application.

Claim Rejections - 35 USC § 112, second paragraph, indefiniteness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 4, 6, 7, 11, 13, 14, 18, 20, 21 and 25 are rejected under 35 U.S.C. 112, second

paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4, 11, 18 and 25 contain the trademark/trade names *Betaseron* and *Avonex*. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, -second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to presumably identify/describe β-interferon and, accordingly, the identification/description is indefinite.

Claims 4, 11, 18 and 25 are indefinite for lacking proper antecedent basis for *Betaseron* and *Avonex*. Claims 4, 11, 18 and 25 depend from independent claims that recite β-interferon which may or may not be different from a *Betaseron* and *Avonex*.

Claims 6, 7, 13, 14, 20 and 21 are indefinite for reciting the phrase "or later" after a definite time point, such as "the 11th day." "Later" has no definite meaning as far as a time course, except "after." The phrase thus encompasses time points any time after administration, including many years after injury, time points that are not enabled (as described below).

Claim Rejections

Claim Rejections - 35 USC § 112, first paragraph - Enablement.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-28 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for a method of treating the secondary damage resulting from spinal cord injury by administering β-interferon at about the 11th day after injury, does not enable a method of treating the secondary damage of spinal cord injury by administering β-interferon later than about 11 days after injury. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with the claims.

The specification does not reasonably provide enablement for use of β-interferon to inhibit secondary damage in the spinal cord later than about 11 days after injury. Independent claims do not specify a time course of administration, while dependent claims recite "11th day *or later*" and "4th week *or later*" after injury. Since "later" can mean any amount of time, even years later, applicants are not enabled for time courses outside such large experimental windows. In addition, evidence provided by applicants would seem to indicate that administration around the 4th week after injury would also be too late to have an effect, as discussed below.

Applicants measured the rise in the numbers of VCAM-1 positive cells in the spinal cord lesion site after an experimental contusion injury in rats (see Figure 5). VCAM-1 levels do not begin to rise until about 8 days after injury, and reach about 2/3 of maximum at 14 days after

injury. VCAM levels are important in that they may be an indicator of leukocyte infiltration, which infiltration applicants contend contributes to the second phase of inflammation. Recent literature seems to support the applicants' hypothesis. There is, for example, increasing evidence that cell-adhesion molecules (CAMS) play a primary role in recruiting leukocytes to sites of injury (Ulbrich, et al, 2003, TRENDS in Pharmacological Science, 24(12): 640-647). In addition, β-interferon has been used to treat multiple sclerosis, where it probably exerts its positive effects on the disease by inhibiting macrophages (Johnson, et al, Scientific American, May 1994, 68-75). It is a reasonable hypothesis in the instant case, that leukocytes contribute to or cause the secondary inflammatory damage seen after spinal cord contusion, since applicants have previously shown that irradiation of the injured site, at radiation levels that kill infiltrating cells but not neurons, decreases inflammation, speeds healing, and improves recovery of myelinating cells (Kalderon & Fuks, 1996, of record, IDS of 26 January 2006).

The instant Application does not reasonably provide enablement for a method of treating secondary damage after a spinal cord injury by administering β-interferon after about 11 days post-injury. Since applicants did not administer β-interferon to the animals after injury, the only evidence that would indicate a time-course for initiation of the secondary damage is the appearance of VCAM-1 positive cells beginning at day eight (Figure 5). This process probably precedes immune cell infiltration, but it is not known precisely *when* macrophages and leukocytes are recruited to the site. In addition, it is not known if the secondary inflammatory process, once begun, is reversible. An irreversible process would also necessitate *early* β-interferon administration, since late administration would obviously have no effect.

Due to the large quantity of experimentation necessary to determine how and when to use β-interferon to treat secondary inflammatory damage after a spinal cord contusion, the lack of direction/guidance presented in the specification regarding same, the absence of working examples in which β-interferon was injected into injured rats, the complex nature of the invention, and the breadth of the claims which fail to recite definite time periods for administration--undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, the specification does not disclose preventing the progressive chronic inflammation, as recited in claim 8 and encompassed by claims 9-14. The term "prevent" is interpreted as meaning that an activity will not occur, i.e. the chronic inflammation and demyelination will not occur. Undue experimentation would be required of the skilled artisan to determine the quantity of β-interferon to be administered, the best route of administration, the duration of treatment, and any possible side-effects to prevent any chronic inflammation or demyelination from occurring.

35 USC § 112, first paragraph – Written Description.

Claims 1-3, 8-10, 15, 16, 17 and 22-24 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 8-10, 15, 16, 17 and 22-24 are directed to methods of treating secondary damage resulting from spinal cord injury by administering β-interferon or an *analogue* thereof. Claims recite use of β-interferon, commercial formulations of β-interferon, and analogues

The specification teaches β-interferon, including commercial formulations. However, the specification does not teach functional or structural characteristics of all β-interferon analogues used for the claimed methods. The description of one peptide species of interferon is not adequate written description of an entire genus of functionally equivalent peptides or non-peptide analogues.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

With the exception of β-interferon referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed analogues, and therefore, would not know how to make and use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The analogue *itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only β-interferon but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion:

Claims 1-28 are rejected for the reasons cited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

29 March 2007

SLW

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER